NATIONAL INSTITUTE OF DIABETES AND DIGESTIVE AND KIDNEY DISEASES

ADMINISTRATIVE GUIDELINES

FOR

CENTERS FOR PKD RESEARCH AND TRANSLATION CORE CENTERS

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I. DESCRIPTION

Background

The NIDDK-supported PKD Research and Translation Core Centers are part of an integrated program of polycystic kidney disease (PKD) research. These Centers were originally established as Specialized Research Centers in 1999. Center grants such as the ICPKD have proven to be a valuable way to promote multidisciplinary interactions and to provide the shared resources needed to address complex biomedical problems, such as therapy of PKD. Centers also can provide the basis for generating technologies that can be applied by other investigators and clinicians in many medical centers throughout the nation. This Centers program is now being enhanced to allow for even more extensive collaboration.

General Description

The objectives of the PKD Research and Translation Core Centers are to bring together basic and clinical investigators from relevant disciplines in a manner which will enhance and extend the effectiveness of their research. In addition to collaborations between scientists within an institution, Core Centers can foster interaction and collaborations between investigators at multiple institutions to promote a multifaceted approach to a common goal. The Core Center consists of several components: a single Administrative Core, several Biomedical Research Cores, and a Pilot and Feasibility Program. A Core Center must be an identifiable unit within a single university, a medical center, or a consortium of cooperative institutions, including an affiliated university. An outstanding existing program of biomedical research in the area of kidney disease, and especially polycystic kidney disease, is required. This research should include NIH-funded research projects and other peer-reviewed research. This established research program must be in existence at the time of submission of a center application. Research programs outside the primary institution where the Core Center is based may utilize the core resources. The base of research projects to be served by the cores must be clearly defined and justified in the application. Efficient management of resources and close cooperation, communication, and collaboration among involved personnel in multiple professional disciplines are ultimate objectives of Core Centers.

Basic Requirements for a P30 Core Center

To be eligible for a Core Center grant, the potential applicant institution must already have a substantial base of ongoing, independently supported, high-quality basic and / or clinical research aimed at the pathophysiology, diagnosis, monitoring, or treatment of PKD. The research base for a Core Center is made up of investigators with individually-funded research projects who can benefit from shared resources. Core Center funding will provide core facilities (shared resources), a Pilot and Feasibility Program (new initiatives), and program enrichment activities. Each Biomedical Research Core within the Center will provide services to Center participants (a detailed description of Biomedical Cores begins on page 8). Except for pilot and feasibility studies, Core Center funds are not intended to support individual biomedical research

projects other than through core usage. The major source of support for biomedical research projects associated with the Center should be derived from separately funded projects of the participating investigators. Similarly, professional trainee stipends are not to be supported through Core Center funding.

A Core Center may serve a single institution or a consortium of institutions engaged in a collaborative approach to PKD research. The Core Center may be based solely at the applicant institution or at multiple institutions through subcontracts. If subcontracts are to be utilized, the applicant must clearly demonstrate how a cohesive and integrated operation will be ensured and describe the advantages of this approach to performance of Core functions. The Core Center may also provide resources for funded projects at collaborating institutions that do not have a sub-contractual arrangement with the parent institution. If such projects are to be included in the research base, the applicant must clearly describe and justify the reasons why it is appropriate for these projects to be included in the research base and the advantages to be derived from the collective utilization of the Core Center.

A new category of Cores that is being encouraged is the Regional/National/International Cores. These Cores serve specific scientific communities on a regional, national, or international level. The research base for cores that are used as a regional, national or international resource should be considered the "extended research base." The extended research base for a regional, national or international core could include all investigators who might expect to use the core in some way. This might include investigators who would be expected to fully compensate the core service through a charge-back, and thus would not be obtaining direct financial assistance from the Center. The list could include investigators who use the core services but otherwise have no collaborative interactions with other Center investigators. The extended research base should be defined as an entity separate from the institutional research base. For review purposes, it should be evaluated as part of the core, in order to distinguish it from the local institutional research base.

At the time of initial submission, the applicant institution or consortium of institutions must have an active program of excellence in basic and clinical biomedical research in the area of polycystic kidney disease. The biomedical research base will be given primary consideration in the peer review process. There should be a focus on basic and clinical research in PKD. Focus, relevance, interrelationships, quality, and to some extent quantity, are all considerations in judging the adequacy of the research base.

II. ADMINISTRATIVE CORE COMPONENT

Description

A PKD Research and Translation Core Center must be an identifiable organizational unit within a university medical center or a consortium of cooperating institutions including the university-affiliated center. Such a Center will involve the interaction of broad and diverse elements; thus, lines of authority and approval by the appropriate institutional officials must be clearly specified.

The administrative core plays a key role in the coordination and functioning of the center.

Requirements

Each applicant institution specifies a Core Center Director to be responsible for the scientific and administrative leadership of the Center. The Director should be an experienced and respected scientist with a proven track record for obtaining NIH funding. He/she must be able to coordinate, integrate, and provide guidance in the establishment of new programs in PKD research. This commitment will require significant effort from the Center Director. Each Center Director is expected to commit at least 2.4 person months to the Center. One or more Associate Directors should be named who will be involved in the administrative, scientific, or training efforts of the center and will serve as Acting Center Director in the absence of the Director. An administrative assistant may also be proposed.

It is expected that the organization of the Administrative core should encompass a supportive structure sufficient to ensure accomplishment of the following:

(1) Coordinating and integrating the Center components and activities

(2) Overseeing the solicitation, review, and selection of pilot and feasibility studies

(3) Reviewing the utilization and quality of core resources

(4) Interacting with the scientific and lay communities and the NIDDK to develop relevant goals for the Center

The final administrative structure of the Center will be left largely to the discretion of the applicant institution (subject to review by NIH peer review mechanisms). However, NIH's experience has demonstrated that the effective development of the Center programs requires close interaction between the Center Director, the principal investigators, appropriate institutional administrative personnel, the staff of the awarding agency, and the members of the community in which the Center is located. Therefore, each Center applicant should establish an administrative structure that will permit the development of such interaction. Within this structure, each applicant institution must also establish a mechanism to oversee the use of funds for the proposed Pilot and Feasibility Program. This mechanism must include review by appropriate consultants from the scientific community outside the Center institution or consortium institutions. Consultants who will serve on advisory committees should not be specifically identified in the application, but the process by which they will be selected should be described. These same consultants may be utilized, if desired, for review of other activities of the Center. The mechanism for reviewing the use of the pilot and feasibility funds will be considered by the initial review groups in the evaluation of the Center applications. Further details regarding this mechanism will be found below in the discussion of the Pilot and Feasibility Program. The projects selected to receive these funds will be described by the Centers in their annual reports and will be reviewed by the NIDDK Staff for eligibility in its annual evaluation of the Center program. Funds for the Pilot and Feasibility Program should be

listed in the Other category in the budget of the Administrative Core. The Center grant may also include limited funds for program enrichment (i.e., seminars, etc.) that should be included in this core.

The initial base of research projects to be served by the cores must be clearly defined in the application. The process by which additional projects will be selected and prioritized to utilize the core resources must be delineated. There should be well defined criteria for designating an investigator as a Center participant. Each Center, however, is expected to formulate these definitions based on its own situation.

Centers need to develop policies and procedures for change of core functions. For example new technologies or services that should be supported might appear; existing technologies might become less important; or economic changes might obviate the need for core services, such as the availability of cost-effective commercial services or core services provided by the research institution. Cores should address the issue of allocation of resources to development of new technologies in comparison to provision of services with existing technologies.

Although facilities available should be described for each element of the application, a more general description of overall facilities and a statement regarding institutional commitment to the Center should also be included here.

III. BIOMEDICAL RESEARCH COMPONENT

Research Base

The Core Center Grant provides a mechanism for fostering interdisciplinary cooperation within a group of established investigators conducting high-quality research on polycystic kidney disease. Therefore, existence of a strong research base in this area is a fundamental requirement for and the most important aspect in the establishment of a Core Center. This research includes NIH-funded research grants (P01, R01, R03, R18, R21, R29, R33, R35, R37, U01, U10, U19, U24, U54, K series awards, and N01). Contracts that primarily fund the production of materials or services for support of research are excluded.

Applicants should include an overview of current PKD-related research being conducted at their institution in sufficient detail to allow reviewers to judge its extent and the interrelationship of ongoing research. There should be a substantial body of ongoing research in PKD. Projects at other institutions may also be included if collaborations exist with scientists at the applicant institutions. Applicants should indicate how the establishment of a Center will provide added dimensions, such as greater focus and increased cooperation, communication, and collaboration.

Presentation of the research base in the application should be done in two ways: (1) by completing a Table like the one shown in Illustration III and (2) by a full description of the PKD-related research activities at the applicant institution and any collaborating institutions. This presentation should be organized into several areas of emphasis that demonstrate the research focus of the Center. These focus areas should include a section on “Basic PKD research” and a section on “Clinical / Translational PKD research.” Additional areas of emphasis relevant to the

goals of the Center may be included. The research of each Center participant should be discussed, and interrelationships of research being conducted by Center participants should be highlighted. Since most, if not all, of the research base will have undergone separate peer reviews, the merit of the individually funded projects is already established. The more important aspects are (1) interactions and interrelationships of the research efforts; (2) uses and benefits of core services; and (3) plans to develop productive collaborations among Center investigators.

The application obviously has insufficient space for a detailed presentation of the research base. However, significant research accomplishments should be cited, and it may be helpful to include a few reprints as examples of the research conducted by Center participants as an appendix to the application. Appropriate presentation of the research base is very important since its assessment is a primary criterion in the evaluation of an application.

For renewal applications, consideration will be given to progress and accomplishments in the research base; to development of multidisciplinary, collaborative, and cooperative interrelationships; and to alteration in the original Center design in order to meet the evolving needs of the research base. This should be described in a narrative fashion and by completing a Table like the one shown in Illustration IV, which documents the contribution of individual cores to the publications by the research base. New areas of research and acquisition of new funding should be highlighted.

Biomedical Research Cores

Definition: A biomedical research core is a shared facility that provides a needed service to Center investigators, enabling them to conduct their funded individual research projects more efficiently and/or more effectively. Cores should be designed to furnish a group of investigators with materials, techniques, determinations, instrumentations, and/or quality control to enhance research and contribute to cost effectiveness. It is acceptable to develop a cost recovery system to help defray costs to the Center. This system would charge a fee to Center participants for services provided by the Core, but at a reduced rate. If such a cost recovery system is developed, a detailed charge justification must be presented and the program income section on the checklist of the PHS 398 must be completed. Participating Center members must also be informed to include such costs with their full budget justifications in their applications for individual grant support. Cores may be proposed to support any research activity of the Center, but usually fall into one of the following categories:

- Collection, storage and distribution of data and samples;
- Provision of specialized tools and technologies or access to specialized expertise;
- Development, standardization, and distribution of reagents and/or protocols;
- Provision of technical assistance, training, and enrichment programs;
- Recruitment of patients and coordination of patient studies;

- Beta-testing and dissemination of specialty assays, methods, and services on an institutional level;
- Increasing interdisciplinary interactions at the institution through cross-project/ laboratory exchange; and
- Sharing of specialized tools, technologies and expertise between collaborating investigators.

Clinical and translational research Cores could provide biostatistical expertise for study design and data management and analysis; bioinformatics support; infrastructure for recruiting and managing clinical research subjects and/or tracking and analyzing clinical samples; technologies useful for phenotyping and characterizing subjects or exploring clinical pathophysiology; and expertise for behavioral assessment or intervention.

Regional/National/International Cores: Centers are encouraged to propose Cores that provide unique resources to a community outside the Institution. These could be on a regional level, a national level, or an international level. A Regional/National/International Core may define its own research base, which is expanded from that of the rest of the Center. The Core may include investigators that just use this resource or service but do not have a formal collaboration with other Center investigators.

Justification for proposing a Core: The establishment and continued support of biomedical research cores within a Center are justified on the basis of use by independently funded Center investigators. The minimum requirement for establishing a Core is significant usage by two or more investigators with independently funded, peer-reviewed projects. While investigators holding awards from the Center's Pilot and Feasibility Program are appropriate users of the Core facilities, their use does not contribute to justification for establishment or continued support of a Core. Additionally, the minimum of two independently funded users does not in itself provide sufficient justification and will receive close scrutiny in review.

Each Core must have in place a procedure to evaluate efficiency and to maintain appropriate quality control. Limited developmental research is an additional appropriate function of a core facility, so long as the research is related directly to enhancing the function or utility of the core and is not an undertaking that should be funded through other mechanisms. The Core should develop policies and procedures for change as technology progresses. Cores must also have well-defined policies to ensure that intellectual property is identified and appropriately protected, but these issues should not impede the sharing of resources. Teaching the investigators and/or their staff members new techniques and methodologies is also an important function of the Cores. The Cores are not intended to supplant investigator capabilities; rather, they are intended to enhance the opportunities of investigators to learn and become proficient in the technologies available through the Core.

Personnel: A director must be named for each Core. A Core Director must contribute at least 0.6 person months. A Core Director with requisite expertise may devote a greater effort to the core and with justification could devote up to 12 person months. Where appropriate, an established expert in the Core activities could also be included as a consultant to the Core.

Technicians, etc., are allowable in accordance with the volume and type of work in the Core.

Facilities, space, and special arrangements: Particularly in initial applications, the description of the physical arrangements and instrumentation for each Core should be given special attention. In renewal applications, any changes should be carefully documented. Cores are encouraged, whenever possible, to enter into cooperative arrangements with established Cores in other Centers or resources offering a similar type of service. However, it should be clear that the PKD Research and Translation Core Centers can function independently.

Management of the Core: The organization and proposed mode of operation of each Core should be presented. A plan for prioritizing investigator use of the Core should be included, as well as a definition of qualified users. If use by investigators outside the parent institution is proposed, the mechanism by which such investigators will apply and be evaluated and selected should be detailed. The definition of qualified users should not be too narrow. Some minor Core use could serve to entice established investigators in other fields into the field of PKD research. Any proposed, ongoing or completed developmental efforts should be described. If the Core is used to train investigators in special techniques, the mechanism for this training should be included.

Relation of Core services to individual research project grants: When a Center is first established, individual investigator-initiated research project grants may include funds for a part of the services that will ultimately be available from the Cores. At the time of renewal (competitive and noncompetitive), the budgets of individual research project grants must be reduced to reflect the costs supported by the Center grant. If there are charge backs, these should be detailed in the submitted budget justification and described as allowable budgetary items in the investigator's individual grants. Some mechanism should be proposed in the Center application to monitor these budgetary adjustments and to ensure that Center Core users describe their relation to the Center in their individual grants.

Renewal applications: Information relative to Cores in renewal applications should generally cover all of the same points as initial applications. In addition, past performance, usage, and accomplishments should be described. The effect of the service provided by a Core on investigator productivity and cost effectiveness should also be addressed.

Pilot and Feasibility Program

Research projects associated with a Core Center will, in general, be funded by other resources, such as grants from NIH, similar project funding from other Federal agencies, or non-Federal sources. The one exception is pilot and feasibility studies.

Definition: A pilot and feasibility study provides modest research support for a limited time (one to two years) to enable eligible investigators to explore the feasibility of a concept related to the mission of the Center and to generate sufficient data to pursue the concept through other funding mechanisms. The pilot and feasibility studies are intended to (1) provide initial support

for new investigators; (2) allow exploration of possible innovative new leads or new directions for established investigators; and (3) stimulate investigators from other areas to lend their expertise to research in this area. Pilot and feasibility study support is not intended for large projects by established investigators that would otherwise be submitted as separate research grant applications. Pilot and feasibility funds are also not intended to support or supplement ongoing funded research of an established investigator**.**

Requirements: Each Center must contain a Pilot and Feasibility Program with a minimum of two projects. A maximum of five projects can be requested. The funds for the Pilot and Feasibility Program are included in the budget of the Center within the $750,000 direct cost cap.

Eligibility and related guidelines: Investigators eligible for pilot and feasibility funding generally fall into three categories: (1) new investigators without current or past NIH research support (R01, P01) as a principal investigator (current or past support from other sources should have been modest); (2) established investigators with no previous work in PKD who wish to apply their expertise to a problem in this area; and (3) established investigators who propose testing innovative ideas that represent clear departure from ongoing research interests. It is expected that the majority of the investigators will fall into the first category. All eligible investigators, however, must have faculty appointments and be independent investigators. Postdoctoral fellows or their equivalent are not eligible. Each pilot and feasibility study proposal should state clearly the justification for eligibility of the investigator under one of the above three criteria.

A proposed pilot and feasibility study should present a testable hypothesis and clearly delineate the question being asked, detail the procedures to be followed, and discuss how the data will be analyzed. It must be on a topic related to the objectives of the Core Center. Projects should be focused, since funding for these studies is modest and is limited to two years. Any one investigator is eligible only once for this support, unless the additional proposed pilot and feasibility study constitutes a real departure from his/her ongoing research.

Pilot and feasibility projects proposing clinical studies are encouraged. The National Center for Research Resources (NCRR) currently supports 46 institutions via Clinical and Translational Science Awards (CTSA), which provide services and resources to enhance clinical research (http://www.ctsaweb.org/). Research Centers supported by the NIDDK are encouraged to collaborate with CTSAs to avoid duplication of effort and enhance utilization of services and resources.

Use a separate Form PHS 398 for each project, and number each project sequentially. Each pilot and feasibility project should be identified clearly by the same title as that provided in the Table of Contents. Each project should begin with an abstract, and budget pages that should be followed by information requested in Sections A through I of the instructions for Form PHS 398. It should be submitted generally using the NIH research project application format, but the research strategy should be limited to six pages.

The application should clearly describe and justify the pool from which potential pilot and feasibility applications will be solicited. This can be limited to investigators at the parent institution or expanded to include investigators at institutions with well defined affiliation with the Center. The mechanisms by which information on the availability of pilot and feasibility awards will be disseminated and by which applicants will apply and be selected for these awards must be described and will be an important element in the review of the pilot and feasibility component of the Center.

Initial review and management of the Pilot and Feasibility Program: By the very nature of this program, a significant responsibility for its management will be left to the Center administration during the project periods. Each Center should include project descriptions for the pilot and feasibility projects they propose to fund. For new Center grant applications, the pilot and feasibility proposals are reviewed for scientific merit and eligibility by the initial review group as an example of the selectivity of the applicant institution's review process. These initial pilot and feasibility studies must have been reviewed by the Center in the manner proposed for review of future studies so that only those considered to be the highest quality are included in the grant application. The recommended budget for the Pilot and Feasibility Program for the first year will be based on the review of the proposed projects. The budget for future years is recommended by the initial review group, based on the quality of the proposed pilot and feasibility studies and the proposed method for management and review (as evidenced by this set of projects). Also considered will be the review group's evaluation of the future justification for continued pilot and feasibility support.

Since pilot and feasibility studies can be awarded for any period of time up to two years, studies end at various times. In addition, the studies may also be terminated by the Center administration before their approved time limit for various reasons: for example, (1) the investigator may receive outside funding for the project; (2) the project was found not to be feasible; (3) the investigator may leave the Center institution; etc. When this occurs, the Center may make new awards for pilot and feasibility studies with the remaining funds.

While a Center's administrative framework for management of the Pilot and Feasibility Program is basically left up to each Center, certain minimal requirements must be met. The program must have a director who is an established investigator in PKD research. There must also be a committee representing all the aspects of the Center that will assist the director in the management of the program. The major responsibilities of the director and the committee should be as follows:

(1) Maintain oversight and review of ongoing pilot and feasibility studies.

(2) Make recommendations regarding termination or other actions to the Center Executive Committee (or equivalent).

(3) Prepare and ensure appropriate distribution of announcements of the availability of pilot and feasibility funding.

(4) Arrange and preside over the scientific merit review of proposals. At least one reviewer from outside the parent institution must be used for each proposal. All reviewers should assign impact/priority scores in accordance with the NIH system. Copies of all of the proposals with written documentation of their reviews, impact/priority scores, and final action must be retained by the Center. These records must be made available to reviewers if requested at the time of a renewal application.

(5) Maintain, insofar as is possible, a record of subsequent career events of each pilot and feasibility study recipient. This record must also be made available to reviewers at the time of the renewal application.

(6) Make recommendations to the Center Executive Committee (or equivalent) for final decisions. A record of actions by this committee must be documented and be available if requested by the initial review group.

All applicants should describe how these requirements will be met and have been met in the case of renewal applications. Also included should be an assessment of the relevancy of the proposed individual pilot and feasibility studies and of the program as a whole to research on PKD and to the specific goals and objectives of the Center program.

Review of the Pilot and Feasibility Program in renewal applications: After the initial review of pilot and feasibility proposals as described above, all responsibility for review and funding during the remainder of the project period will reside within the Center itself. This approach provides each Center with the needed flexibility for effective and efficient management of the program. In competing renewal applications, the review of this program will be based on the past track record, the management of the program, and an assessment of overall potential needs and opportunities.

In general, a competing renewal application will include the following:

(1) an historical overview;
(2) a description of Center management of the program;
(3) a description of the method for solicitation for pilot and feasibility projects and the number of respondents received for each solicitation;
(4) a listing of all previous, ongoing and approved proposed pilot and feasibility studies with reports on those which were supported by the Center during the last project period; and
(5) a statement relating to benefits of the program to the Center as well as the contribution of the uniqueness of the Center environment to the program.

These points are detailed in the following paragraphs.

The historical overview will cover the Pilot and Feasibility Program since the inception of the Center. This should include, in summary format, all pilot and feasibility projects ever awarded. For each project listed, the following should be included:

(1) publications as a result of the studies;
(2) peer-reviewed funding as a result of the studies; and

(3) whether the recipient is still active in the area of PKD.

The Pilot and Feasibility Program Director may wish to highlight certain studies or certain aspects of the past studies. Collaborations that resulted in lasting relationships, acquisition of new skills by the study recipient, or other significant outcomes should be identified. The relationship of the scope of the various studies to that of the Center should be emphasized. Details such as back-up documentation (described earlier in relation to the arrangement of the Pilot and Feasibility Program) should not be included, but should be available for examination by the reviewers if requested.

The description of Center management of the program will present in detail the current system used to manage the Pilot and Feasibility Program, including its integration with and relationship to the rest of the administrative structure. The use of outside consultants for review should be included in the discussion. Important features of the solicitation process should be provided, including the distribution and the number of respondents.

The description of the accomplishments of the Pilot and Feasibility Program should include a list of all NIDDK-supported pilot and feasibility studies awarded. For each pilot and feasibility project awarded during the last project period, include a brief report (1-2 pages) containing

(1) the name of the investigator, degree(s), professional career status at the time awarded, and current professional career status (if known);
(2) an overview of the project, including its significance and salient results;
(3) a list of resulting publications; and
(4) peer-reviewed subsequent funding in the same or related area.

The proposals should be available, if requested by the initial review group.

Funding levels for the Pilot and Feasibility Program on renewal applications: The format for renewal of Pilot and Feasibility Programs will depend on whether the applicant is requesting (1) a number of pilot projects less than or equal to that for the previous project period or (2) an increase in the number of pilot projects.

If the applicant wishes to maintain the same number of pilot projects in a renewal application, the recommendation of the initial review group will be based on the overall performance of the Center's Pilot and Feasibility Program as documented in the application. This recommendation will be based on

(1) the extent to which awarded funds were fully utilized during the previous project period;
(2) awards made to investigators who fully met the eligibility criteria for pilot and feasibility support as outlined above;
(3) Center-relatedness; and
(4) success of previously supported pilot and feasibility studies (e.g., publications, subsequent independent R01 or other peer-reviewed support, and/or attraction of new investigator into Center related research).

Conversely, should the applicant institution feel that an increased level of funding for the Pilot and Feasibility Program is justified, new pilot and feasibility studies, over and above the number currently awarded, must be submitted with the competing renewal application. These proposals

would be reviewed by the initial review group in a fashion similar to the review of pilot and feasibility studies during the initial review. The initial review group would assess the new proposals, along with the overall performance of the program during the previous grant period to arrive at a recommendation for a possible increased pilot and feasibility funding level.

Educational Enrichment Programs

The establishment of a Center should provide an enhanced environment for research training. Students, fellows, and junior faculty should be encouraged to take full advantage of all Center-sponsored seminars, courses, workshops, and symposia. If appropriate, Centers may waive fees for attendance at such events for interested students, fellows, and junior faculty members. Enrichment program-sponsored mini-sabbaticals, or other instructional opportunities, also may be appropriate for postdoctoral fellows. Stipends for fellows are never an allowable Center expense, but travel, per diem, and registration expenses may be paid from enrichment program funds.

Just as in the case of funding for individual research projects, funding for fellowships should be sought from NIH NRSA institutional training grants (T32) and individual fellowships (F32, F33), and other sources, such as the PKD Foundation, other private foundations, and commercial companies.

Although no budgetary items would be included for research training, a section should be included in both initial and competing renewal applications documenting the research training program in cystic fibrosis, its relationship to the Center, and how the presence of the Center may enhance the program.

IV. PRE-APPLICATION PROCESS

Within the limits of available funding, the Centers have been established to meet a national need. Applications will be received in response to RFAs announced in the NIH Guide for Grants and Contracts. It is strongly encouraged that potential applicants for the Centers submit a letter of intent. The letter should be sent at least one month before submission to allow NIDDK staff to identify potential opportunities and problems early in the development of the application. The letter of intent needs to include only the following:

(1) names of the principal investigators and principal collaborators,
(2) identification of the organization(s) involved; and
(3) the announcement to which the potential application is responsive.

The purpose of the letter of intent is to establish communication between the potential applicant group and NIDDK staff. It is not part of the peer review material. Upon receipt of the letter, the appropriate NIDDK program director contacts the prospective principal investigator to assist in a number of areas that include scientific content and objectives, organization, and clarifications. However, applicants should not construe advice given by the NIDDK staff as assurance of favorable review. The staff will not evaluate or discuss the merit of the scientific aspects of the proposal.

V. PREPARATION OF APPLICATION

Description

Applications must be prepared using the PHS 398 research grant application instructions and forms (rev. 11/2007). Applications must have a DUN and Bradstreet (D&B) Data Universal Numbering System (DUNS) number as the Universal Identifier when applying for Federal grants or cooperative agreements. The DUNS number can be obtained by calling (866) 705-5711 or through the website at http://www.dunandbradstreet.com/. The DUNS number should be entered on line 11 of the face page of the PHS 398 form. The PHS 398 document is available at http://grants.nih.gov/grants/funding/phs398/phs398.html in an interactive format. For further assistance contact GrantsInfo, Telephone (301) 435-0714, Email: GrantsInfo@nih.gov.

USING THE RFA LABEL: The RFA label available in the PHS 398 (rev 11/2007) application form (see website above) must be affixed to the bottom of the face page of the original copy of the application. Type the RFA number on the label. Failure to use this label could result in delayed processing of your application such that it may not reach the review committee in time for review. In addition, the RFA title and number must be typed on line 2 of the face page of the application form and the YES box must be marked. The RFA label is also available at http://grants.nih.gov/grants/funding/phs398/labels.pdf

SENDING AN APPLICATION TO THE NIH: Submit a signed, typewritten original of the application, including the Checklist, plus three signed photocopies, in one package to:

CENTER FOR SCIENTIFIC REVIEW
NATIONAL INSTITUTES OF HEALTH
6701 ROCKLEDGE DRIVE, ROOM 1040 - MSC 7710
BETHESDA, MD 20892-7710
BETHESDA, MD 20817 (for express/courier service)

At time of submission, two additional copies of the application must be sent to:

CHIEF, REVIEW BRANCH
NIDDK, DIVISION OF EXTRAMURAL ACTIVITIES
DEMOCRACY 2, ROOM 752 MSC 5452
BETHESDA, MD 20892-5452

The arrangement of materials should follow both the instructions in the PHS Form 398 application kit and the more specific guidance detailed below.

Applicants should keep in mind that the written application is the basis for the merit review. Particular attention should be given to the format of the application. Awards for Center grants will be made only for five-year project periods. Some basic information useful for preparing the application follows. Applicants may also consult with NIDDK staff concerning the technical

aspects of preparing the application.

Content Order for Applications

SECTION 1: INTRODUCTION

- Face Page. The RFA label must be affixed to the bottom of the face page and the title, "Centers for Polycystic Kidney Disease Research" and the RFA number must be typed on line 2 and the YES box must be marked.

- Description and Key Personnel

- Table of Contents

- Budgets
    1. Detailed Budget for Initial Budget Period
    2. Budget for Entire Proposed Project Period
    3. Consolidated budget for first year of requested support (e.g., Illustration I)

- Biographical Sketches for all Center participants beginning with Center Director and Associate Director and the rest in alphabetical order

- Distribution of Professional Effort on this Center application (e.g., Illustration II)

- Summary of total current and pending support of all Center participants, including percent efforts. List support related to Basic PKD Research first, followed by Clinical PKD Research and then non-Center-related research support. (e.g., Illustration III)

- General description of the proposed or established Center
  For Renewals: Changes from the original Center design should be highlighted

SECTION 2: ADMINISTRATIVE COMPONENT

- Budget Page with comprehensive budgetary justifications (PHS 398 form page 4 Rev. 11/2007)

- Qualifications of the Director and Associate Director

- Presentation of the administrative structure

- Relationship and lines of authority and sanction by appropriate institutional officials

- Committee structure (include committee for the Pilot and Feasibility Program)
- General overall description of facilities and institutional commitment
- Description of plans for the enrichment program
- Other considerations

SECTION 3: BIOMEDICAL RESEARCH COMPONENT

- Overview of ongoing research and impact of Center on this research.
  Description of Research Base—Grouped into areas of emphasis for the Center
  For Renewals: Progress Report including description of significant findings, new participants and new funding
- For Renewals: Publications Citing Support from this Center (e.g., Illustration IV)
- Biomedical research cores (present each core separately)
    1. Descriptive abstract
    2. Budget with justifications (PHS 398 form 4 (rev. 11/2007))
    3. Objectives of the core
    4. Core function, including quality control
    5. Benefits from core
    6. Proposed developmental research or training
    7. Investigators who will use the core and proposed extent of use (e.g., Illustration V)
    8. For Renewal: Core use during the last grant period (e.g., Illustration V)
    9. Vertebrate Animal and or Human Subjects Sections if appropriate
- Pilot and Feasibility Program
    1. Composite budget with budgetary justifications for future years

2. Introduction

3. Director and Committee

4. Management of the Pilot and Feasibility Program

5. Description of the Pilot and Feasibility Program

6. In initial applications include budget and justifications, justification of eligibility, as well as the scientific proposals with their justification for core usage.

7. For competing renewal applications, also include overview; listing and reports of pilot and feasibility studies; and additional pilot and feasibility proposals, if applicable, as requested for an initial application.

- Research Training Program

    1. Description

    2. Other considerations

- Checklist

VI. BUDGET CONSIDERATIONS

Unless otherwise indicated in the Notice of Grant Award, allowable costs and policies governing the research grant program of the NIH will prevail. The anticipated award will be for five years. The annual direct costs requested may not exceed $750,000. Each pilot/feasibility study is limited to $50,000 per year and a two-year duration of support. An exception to the $750,000 cap will apply to Center applications that include subcontracts. Subcontract facilities and administrative costs are not included in the direct cost cap of $750,000 (Notice OD-04-040; http://grants2.nih.gov/grants/guide/notice-files/NOT-OD-04-040.html). Equipment may be included in the first year of the grant, which will not be included in the direct cost cap.

Budget Categories

Professional Personnel: This category may include support for salaries of key personnel within the Center who contribute to allowable activities of the Center. The salaries derived from the Center grant will depend on the effort provided and institutional salary as well as existing NIH policies; however, current NIDDK practice limits annual increments to 3 percent. The Center Director is expected to devote at least 20 percent of his or her efforts to the Center. The Center

application should include salaries for individual principal investigators only to the extent that they provide an essential Center function. No overlap of time or effort between the Center and separately funded projects is permitted.

Salaries of professional personnel engaged in research activities supported by pilot and feasibility funds of the Center are an allowable cost item, as are salaries of professional personnel in core facilities.

Technical and Support Personnel: This may include salaries for identified positions to be filled in the Center. No overlap of time or effort between the Center and separately funded projects is permitted.

Equipment: Requests for large equipment costs must include documentation of similar equipment already available at the institution and provide a clear justification in terms of core need and service to Center investigators. General purpose equipment needs should be included only after surveying the availability of such items within the institution.

Supplies: Consumable supplies related to the operation of the Center are allowed and include office materials, as well as scientific supplies, but should not be to supplement separately funded projects.

Research Patient Care Costs: Research patient care costs (both in-patient and out-patient expenses) will be considered in the context of other existing institutional clinical resources. Attempts should be made by the applicant institution to utilize existing clinical facilities, such as General Clinical Research Centers and individually supported beds. Costs relating to the clinical research efforts of Center investigators may be funded through the Center, provided there is no overlap of funding. The Center is not intended to be a facility for health care delivery; thus, only those patient costs directly related to research activities may be charged to the Center.

Travel: Domestic and foreign travel of project personnel directly related to the activities of the Center is allowable. Travel of Center participants for attendance at annual Center directors meetings is allowable.

Consultants: Consultants and any associated costs (consultant fees, per diem, travel) may be included when their services are required within the Center**.**

VII. REVIEW PROCESS AND CRITERIA

Upon receipt, applications will be initially reviewed for completeness by the Center for Scientific Review (CSR). Incomplete applications will not be reviewed. Evaluation of responsiveness to the program requirements and criteria stated in the RFA is an NIDDK staff function.

Those applications that are complete and responsive will be evaluated, in national competition, for scientific/technical merit by an appropriate peer review group convened by the NIDDK in

accordance with the criteria stated below. It is essential that the written application be in a form to be reviewed on its own merit, since no site-visit is anticipated. Following this review, the applications will be given a second level review by the National Diabetes and Digestive and Kidney Diseases Advisory Council.

The initial review group will review each application using the criteria stated below:

- **Overall Impact**. Reviewers will provide an overall impact/priority score to reflect their assessment of the likelihood for the project to exert a sustained, powerful influence on the research field(s) involved, in consideration of the following five core review criteria, and additional review criteria (as applicable for the project proposed).

- **Core Review Criteria**. Reviewers will consider each of the five review criteria below in the determination of scientific and technical merit, and give a separate score for each. An application does not need to be strong in all categories to be judged likely to have major scientific impact. For example, a project that by its nature is not innovative may be essential to advance a field.

- **Significance**. Does the project address an important problem or a critical barrier to progress in the field? If the aims of the project are achieved, how will scientific knowledge, technical capability, and/or clinical practice be improved? How will successful completion of the aims change the concepts, methods, technologies, treatments, services, or preventative interventions that drive this field? What are the strengths of the Center's research base (its breadth and depth) and the relevance and interrelation of these separately funded research projects to the PKD focus of the Center? How appropriate and relevant are the proposed Cores and their modes of operation (such as, how usage will be prioritized)? What is the potential for Core contribution to ongoing research? Are there at least two users identified for each Core?

- **Investigator(s)**. Are the PD/PIs, collaborators, and other researchers well suited to the project? If Early Stage Investigators or New Investigators, do they have appropriate experience and training? If established, have they demonstrated an ongoing record of accomplishments that have advanced their field(s)? If the project is collaborative or multi-PD/PI, do the investigators have complementary and integrated expertise; are their leadership approach, governance and organizational structure appropriate for the project? Are the Center investigators willing to interrelate with each other and contribute to the overall objectives of the PKD Core Center? What are the scientific and administrative leadership abilities of the proposed Center Director and Associate Director and their commitment and ability to devote adequate time to the effective management of the program? Is appropriate administrative organization proposed for the following:(a) Coordination of ongoing research between the separately funded projects and the Center, including mechanisms for internal monitoring;(b) Establishment and maintenance of internal communication and cooperation among the Center investigators;(c) Mechanism for

selecting and replacing professional or technical personnel within the Core Center;(d) Mechanism for reviewing the use of and administering funds for the P&F program;(e) Management capabilities that include fiscal administration, procurement, property and personnel management, planning, budgeting, and other appropriate capabilities?

- **Innovation**. Does the application challenge and seek to shift current research or clinical practice paradigms by utilizing novel theoretical concepts, approaches or methodologies, instrumentation, or interventions? Are the concepts, approaches or methodologies, instrumentation, or interventions novel to one field of research or novel in a broad sense? Is a refinement, improvement, or new application of theoretical concepts, approaches or methodologies, instrumentation, or interventions proposed? Are two to five Pilot & Feasibility (P&F) studies submitted for evaluation as part of the review of the P&F program? Are the P&F applicants eligible and is there an adequate selection process by which the individual studies were selected?

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  - **Approach.** Are the overall strategy, methodology, and analyses well-reasoned and appropriate to accomplish the specific aims of the project? Are potential problems, alternative strategies, and benchmarks for success presented? If the project is in the early stages of development, will the strategy establish feasibility and will particularly risky aspects be managed? If the project involves clinical research, are the plans for 1) protection of human subjects from research risks, and 2) inclusion of minorities and members of both sexes/genders, as well as the inclusion of children, justified in terms of the scientific goals and research strategy proposed?

  - **Environment.** Will the scientific environment in which the work will be done contribute to the probability of success? Are the institutional support, equipment and other physical resources available to the investigators adequate for the project proposed? Will the project benefit from unique features of the scientific environment, subject populations, or collaborative arrangements? Is there institutional commitment to the program, including lines of accountability regarding management of the Center grant and the institution's contribution to the management capabilities of the Center? Is there clear potential for interaction with scientists from other departments and institutions? Although the Center does not specifically support research training, is there demonstration of accomplishments and future plans related to the training of investigators necessary to conduct research in PKD? Is there integration of these efforts into the overall Center, including core facilities? Is there efficient and effective use and/or planned use of the limited enrichment funds, including the contribution of these activities in enhancing the objectives of the Center?

For new applications, the Pilot and Feasibility Program is judged on the basis of: (1) scientific merit of the studies as submitted (based on criteria above), and (2) the merit of the administrative process for selecting subsequent studies.

In competing renewal applications, emphasis is placed on the Pilot and Feasibility Program as a whole, including past track record and management of the program.

In addition to the above criteria, in accordance with NIH policy, all applications will also be reviewed with respect to the following:

Additional Review Criteria. As applicable for the project proposed, reviewers will consider the following additional items in the determination of scientific and technical merit, but will not give separate scores for these items.

Protections for Human Subjects. For research that involves human subjects but does not involve one of the six categories of research that are exempt under 45 CFR Part 46, the committee will evaluate the justification for involvement of human subjects and the proposed protections from research risk relating to their participation according to the following five review criteria: 1) risk to subjects, 2) adequacy of protection against risks, 3) potential benefits to the subjects and others, 4) importance of the knowledge to be gained, and 5) data and safety monitoring for clinical trials. For research that involves human subjects and meets the criteria for one or more of the six categories of research that are exempt under 45 CFR Part 46, the committee will evaluate: 1) the justification for the exemption, 2) human subjects involvement and characteristics, and 3) sources of materials.

Inclusion of Women, Minorities, and Children. When the proposed project involves clinical research, the committee will evaluate the proposed plans for inclusion of minorities and members of both genders, as well as the inclusion of children.

Vertebrate Animals. The committee will evaluate the involvement of live vertebrate animals as part of the scientific assessment according to the following five points: 1) proposed use of the animals, and species, strains, ages, sex, and numbers to be used; 2) justifications for the use of animals and for the appropriateness of the species and numbers proposed; 3) adequacy of veterinary care; 4) procedures for limiting discomfort, distress, pain and injury to that which is unavoidable in the conduct of scientifically sound research including the use of analgesic, anesthetic, and tranquilizing drugs and/or comfortable restraining devices; and 5) methods of euthanasia and reason for selection if not consistent with the AVMA Guidelines on Euthanasia.

Renewal Applications. When reviewing a Renewal application (formerly called a competing continuation application), the committee will consider the progress made in the last funding period. Do Renewal applications document the use, utility, quality control, and cost effectiveness of each Core requested to continue as part of the Center? Is there a significant list of publications arising from the Cores? For Renewal applications, are data supplied on the success of previously funded P&F projects in obtaining outside support?

Biohazards. Reviewers will assess whether materials or procedures proposed are potentially

hazardous to research personnel and/or the environment, and if needed, determine whether adequate protection is proposed.

Additional Review Considerations. As applicable for the project proposed, reviewers will address each of the following items, but will not give scores for these items and should not consider them in providing an overall impact/priority score.

Budget and Period Support. Reviewers will consider whether the budget and the requested period of support are fully justified and reasonable in relation to the proposed research.

Select Agents Research. Reviewers will assess the information provided in this section of the application, including 1) the Select Agent(s) to be used in the proposed research, 2) the registration status of all entities where Select Agent(s) will be used, 3) the procedures that will be used to monitor possession use and transfer of Select Agent(s), and 4) plans for appropriate biosafety, biocontainment, and security of the Select Agent(s).

Resource Sharing Plans. Reviewers will comment on whether the following Resource Sharing Plans, or the rationale for not sharing the following types of resources, are reasonable: 1) Data Sharing Plan (http://grants.nih/gov/grants/policy/data_sharing/data_sharing_guidance.htm); 2) Sharing Model Organisms (http://grants.nih.gov/grants/guide/notice-files/NOT-OD-04-042.html); and 3) Genome Wide Association Studies (GWAS) (http://grants.nih.gov/grants/guide/notice-files/NOT-OD-07-088.html).

VIII. AWARD CRITERIA

Funding decisions will be based on the quality of the proposed Center as determined by peer review, overall balance in the PKD Center program, and the availability of funds.

IX. EVALUATION AND REPORTING REQUIREMENTS

NIH will make information on due dates for the annual Non-Competing Grant Progress Report (PHS FORM 2590) accessible electronically. Forms for PHS 2590 are available at http://grants1.nih.gov/grants/funding/2590/2590.htm. For more information about electronic notification see http://grants.nih.gov/grants/guide/notice-files/NOT-OD-02-047.html

X. SPECIAL CONSIDERATIONS

While each Center will be expected to develop its own program in accordance with local talents, interests, and resources, each must be responsive to national needs to develop therapies for polycystic kidney disease and must be willing to work with the NIDDK and other organizations in furthering the overall goals of the PKD Centers Program. In this regard, the Center Director and selected other Center participants may be invited to meet periodically with NIDDK staff and its consultants to review progress, identify emerging needs and opportunities, and plan approaches for future investigations.

Within the context of these guidelines, potential applicants for Center grants are encouraged to exercise the flexibility necessary to utilize the strengths of their particular institutions in preparing a plan that will eventually cover the spectrum of required activities. Although types of activities that should be included are indicated in the guidelines, specific approaches for their accomplishment are left to the individual applicant.

Because of resource limitations, and in light of the size of the Center grants, it is unlikely that NIDDK will be in a position to provide hardship allowances in the event that an application for renewal of Center support is not funded.

ILLUSTRATION I
CONSOLIDATED BUDGET FOR FIRST YEAR OF REQUESTED SUPPORT

Budget Category	Admin	Core A	Core B	Core C	Core D	Total
Personnel						
Consultant Costs						
Equipment						
Supplies						
Domestic Travel						
Foreign Travel						
Patient Care Costs						
Alterations and Renovations						
Other Expenses						
Contractual Costs						
Total						

ILLUSTRATION II

DISTRIBUTION OF PROFESSIONAL EFFORT ON THIS APPLICATION

Participating Investigators*	Admin	Core A	Core B	Core C	P and F	Application Total	Other Support
Dr. A.	*1.2			1.2		2.4	6.0
Dr. B.		1.2			*1.2	2.4	4.8
Dr. C.	0.6					0.6	
Dr. D.			1.8	*1.2		3.0	6.6
Etc.							

***Star the effort level (See Admin) when that individual is the core director or the principal investigator on a pilot and feasibility study. Minimum effort for Core Director is 0.6 person months. Minimum total effort for Center Director is 2.4 person months.**

ILLUSTRATION III

SUMMARY OF TOTAL CURRENT AND PENDING SUPPORT OF ALL CENTER PARTICIPANTS

Principal Investigator Co-Investigator*	Supporting Organization and Grant Number	Title	Project Period	Current Annual Amount	Effort Level
BASIC PKD RESEARCH BASE **Current Support**					
Example: Doe, John	P01 DK00000	Murine Models of PKD	4/1/99-3/31/04	$500,000	4.8
Smith, Lisa (Doe, John)	K08 DK00000	Genomic Instability in PKD	6/1/01-5/31/05	$75,000	6.0
Jones, Steve	R01 DK00000	ADPKD Genetics	7/1/01-6/30/06	$200,000	1.8
Pending Support					
Principal Investigator Co-Investigator	**Supporting Organization and Grant Number**	**Title**	**Project Period Requested**	**First Year Support Requested**	**Effort Level Requested**

CLINICAL / TRANSLATIONAL PKD RESEARCH BASE
Current Support
(as above)
Pending Support
(as above)

NON-CENTER-RELATED RESEARCH SUPPORT
Current Support
(as above)
Pending Support
(as above)

- **If co-investigator's name is used, put principal investigator's name in parentheses below.**

ILLUSTRATION IV - FOR COMPETING RENEWALS ONLY

PUBLICATIONS CITING SUPPORT FROM THIS CORE CENTER GRANT

Contributing Cores

Core Number and P.I. Name	Publications	Core 1	Core 2	Core 3	Core 4	P & Fs
1. Doe, J	Doe, J; Jones, S.; Smith, L. JAK-STAT signaling in PKD. Cell, 2001	P		S		
	Doe, J.; Jones, S.; Brown, P. Murine models Of PKD. Am J Physiol Renal Physiol, 2003	P	S			S
2. Jones, S.	Jones, S.; Black, L. Treatment of ADPKD Nature Medicine, 2004.	S	P			S
	Smith, L.; Jones, S.; Defining ADPKD phenotypes AJKD, 2003		P	S		S

***List each publication only once under the project number most significantly contributing to the work. The project most significantly contributing to the work should be signified by P (primary). All other contributing projects and cores are designated by S (secondary).**

ILLUSTRATION V
USE OF CORE FACILITIES

CORE: NAME

Determination/Services Rendered

A.

B.

Users	Funded Projects with Identifying Number	Period of Performance	Determinations/ Services	Estimated Use and Comments
1.				
2.				
3.				

EXAMPLE

CORE: Transgenic Animals

Determination/Services Rendered

A.

B.

C.

D.

Users	Funded Projects with Identifying Number	Period of Performance	Determinations/ Services A B C D E	Estimated Use and Comments
1. J. Doe	R01 DK00000-00	3/7/97-3/7/98	X X	A. 5 per month for 12 months
2. L. Smith	K08 DK00000-00	1/4/97-1/4/00	C. 100 per month X	B. 40 per week through 1/4/00
3. S. Jones	R01 GM00000-00	9/1/01-2/1/02	X	A. 16 per week for 6 months